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EXAMINER	
DUFFY, BRADLEY	

ART UNIT	PAPER NUMBER
1643	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/736,188	BOWDISH ET AL.	
	Examiner	Art Unit	
	Brad Duffy	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-11,13-17,19-23 and 25-55* is/are pending in the application.

4a) Of the above claim(s) *4,5,10,11,16,17,22 and 23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,7-9,13-15,19-21 and 25-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 December 2003 and 23 August 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :5/22/06,10/2/06,10/16/06,3/5/07.

DETAILED ACTION

1. The amendment filed May 11, 2007 is acknowledged and has been entered. Claims 1 and 49 have been amended.

2. The election with traverse filed May 11, 2007, is acknowledged and has been entered.

Applicants has elected to prosecute the invention of the Group I, claims 1-3, 25-30, 49 and 52, drawn to a method of determining whether OX-2/CD200 is upregulated in a subject and administering to those subjects in which CD200 is upregulated a polypeptide that binds OX-2/CD200, and Groups B and E, wherein the polypeptide administered comprises an antibody comprising a light chain CDR1 region with the amino acid sequence of SEQ ID NO:12, a light chain CDR2 region with the amino acid sequence of SEQ ID NO:23, a light chain CDR3 region with the amino acid sequence of SEQ ID NO:37, a heavy chain CDR1 region with the amino acid sequence of SEQ ID NO:55, a heavy chain CDR2 region with the amino acid sequence of SEQ ID NO:74 and a heavy chain CDR3 region with the amino acid sequence of SEQ ID NO:93.

3. Claims 1-5, 7-11, 13-17, 19-23 and 25-55 are pending. Claims 4, 5, 10, 11, 16, 17, 22 and 23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on May 11, 2007.

4. Due to the rejoinder detailed below, claims 1-3, 7-9, 13-15, 19-21 and 25-55 are under examination.

Request to Change Inventorship under 37 CFR 1.48(a)

5. In view of the papers filed March 19, 2007, it has been found that this nonprovisional application, as filed, through error and without deceptive intent,

improperly set forth the inventorship, and accordingly, this application has been corrected in compliance with 37 CFR 1.48(a). The inventorship of this application has been changed by the addition of Anke Kretz-Rommel.

Response to Amendment

6. The amendment filed on May 11, 2007, is considered non-compliant because it fails to meet the requirements of 37 CFR § 1.121, as amended on June 30, 2003 (see *68 Fed. Reg. 38611*, Jun. 30, 2003). However, in order to advance prosecution, rather than mailing a Notice of Non-Compliant Amendment, Applicant is advised to correct the following deficiencies in replying to this Office action:

The amendment to the claims is non-compliant because while claims 56-70 are correctly identified with the status identifier of "Not Entered", these claims fail to comply with 37 CFR § 1.121 (c)(4)(i). Notably 37 CFR § 1.121 (c)(4)(i) states: "No claim text shall be presented for any claim in the claim listing with the status of "canceled " or "not entered" ". Therefore, as claims 56-70 improperly present claim text these claims fail to comply with 37 CFR § 1.121 (c)(4)(i).

Additionally, the amendment to the claims is non-compliant because it incorrectly and improperly lists the status of claims 4-5, 7-11, 13-17, 19-23, 31-48, 50-51 and 53-55 as "withdrawn". Notably, none of the claims were withdrawn at the time the amendment was filed. Although claims 4, 5, 10, 11, 16, 17, 22 and 23 have now been withdrawn, the status of the other claims is incorrect.

Finally, in response to Applicant's request at page 12 and 14 of the response filed May 11, 2007 that claims 56-70 be entered and subjected to a new restriction requirement, it is noted that in the Notice mailed April 11, 2007 at page 3 that the Examiner requested that the Applicant properly add claims if Applicant desired to have the Office consider claims directed to an invention not encompassed by the originally presented claims. The Examiner further provided that since claims 56-70 were not entered, that claims 56-70 should properly be identified as "Not Entered" and any new

claims for consideration should be numbered starting at claim 71. Therefore, since claims 56-70 were not entered, they cannot be entered by the Examiner now and subjected to a new restriction requirement.

Applicant is reminded: Only the corrected section(s) of the non-compliant amendment must be resubmitted (in its entirety), e.g., the entire "Amendments to the claims" section of applicant's amendment must be re-submitted. 37 CFR § 1.121(h).

Election/Restrictions

7. Upon further consideration of the restriction and election requirement set forth in the Office action mailed July 26, 2006, the methods of Group III have been rejoined with the methods of Group I, as both groups comprise methods for treating subjects comprising determining whether OX-2/CD200 is upregulated in a subject and administering a polypeptide that binds to OX-2/CD200 to those subjects in which OX-2/CD200 is upregulated. The restriction and election requirement separating these inventions has been withdrawn.

Thus, claims 1-3, 7-9, 13-15, 19-21 and 25-55 are under examination, insofar as they are drawn to methods for treating subjects comprising determining whether OX-2/CD200 is upregulated in a subject and administering a polypeptide that binds to OX-2/CD200 to those subjects in which OX-2/CD200 is upregulated, wherein the polypeptide administered comprises an antibody comprising a light chain CDR1 region with the amino acid sequence of SEQ ID NO:12, a light chain CDR2 region with the amino acid sequence of SEQ ID NO:23, a light chain CDR3 region with the amino acid sequence of SEQ ID NO:37, a heavy chain CDR1 region with the amino acid sequence of SEQ ID NO:55, a heavy chain CDR2 region with the amino acid sequence of SEQ ID NO:74 and a heavy chain CDR3 region with the amino acid sequence of SEQ ID NO:93.

8. Applicant's traversal of the restriction and election requirement set forth in the Office action mailed July 26, 2006, is acknowledged.

Applicant's arguments have been carefully considered but have not been found persuasive for the following reasons:

The traversal is on the following grounds: "Restriction between groups of claims or sequences is proper only if a search of the groups or sequences together would place an unreasonable search burden on the examiner. In this case, a search of Groups A and D, B and E, and C and F, would not pose an undue search burden on the Examiner. These Groups describe the light chain CDRs (Groups A, B, and C) and the heavy chain CDRs (Groups D, E, and F) of three antibodies that specifically bind OX-2/CD200. As these antibodies bind to the same antigen, a search of all three antibodies would not pose an undue search burden on the Examiner, regardless of any structural differences that may exist among the antibodies. Accordingly, a restriction between the SEQ ID NOS is improper" (page 14, paragraph 4, of the response filed May 11, 2007).

Contrary to Applicant's assertions, the inventions are patentably distinct for the reasons set forth in the Office action mailed July 26, 2006, and because they are so distinct, the search necessary to examine claims directed to any one of the inventions is not the same, nor is it coextensive with the search required to examine claims directed to any other. Notably, the disclosed antibodies comprise different CDR sequences and as such would have different functional properties (e.g., different affinities for a OX-2/CD200 polypeptide or different abilities to treat patients to name two). Furthermore, as each antibody comprises CDRs with different amino acid sequences, different sequence searches within up to 10 different databases are required to consider each antibody which presents an undue burden on the Patent and Trademark Office due to the complex nature of the search in terms of computer time needed to perform the search and the subsequent analysis of the search results by the Examiner. Therefore, since different searches must be performed and different non-prior art issues must be considered to examine claims directed to each of the different antibodies used in the methods, a need to search and consider more than one antibody would constitute a serious burden.

Finally, Applicant has provided no evidence to establish why the remaining groups are sufficiently related or why the requirement for restriction is improper. Clearly different searches and issues are raised in the examination of each group, which would create a burden on the Office. See MPEP 808.02.

Beyond the rejoinder of Group III with the elected invention, the restriction and election requirement set forth in the Office action mailed July 26, 2006, is deemed proper and therefore made FINAL.

Information Disclosure Statement

9. The references cited in the information disclosure statements filed on May 22, 2006, October 2, 2006, October 16, 2006 and March 5, 2007 have been considered.

Specification

10. The disclosure is objected to because of the following informalities:

(a) The specification is objected to because the use of improperly demarcated trademarks has been noted in this application. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks. See MPEP § 608.01(v).

Examples of such improperly demarcated trademarks appearing in the specification are Sepahrose™ and Histopaque™ (see pages 7 and 19).

Appropriate correction is required. Each letter of a trademark should be capitalized or otherwise the trademark should be demarcated with the appropriate symbol indicating its proprietary nature (e.g., ™, ®), and accompanied by generic terminology. Applicants may identify trademarks using the "Trademark" search engine under "USPTO Search Collections" on the Internet at <http://www.uspto.gov/web/menu/search.html>.

(b) The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is

requested in correcting any errors of which applicant may become aware in the specification.

Appropriate correction is required.

Claim Objections

11. Claims 7-9, 13-15, 19-21, 25-48 and 53-55 are objected to as being drawn to the subject matter of non-elected inventions.

Claim Rejections - 35 USC § 112

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 1-3, 7-9, 13-15, 19-21 and 25-55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claims 1-3, 7-9, 13-15, 19-21 and 25-55 are indefinite because of the use of the term "OX-2/CD200" or "CD200". The use of the term "OX-2/CD200" or "CD200" to identify the protein to which the claims are directed renders the claims indefinite because it fails to point out with the requisite clarity and particularity the identity of the protein. Different laboratories often use the same nomenclature to identify structurally and/or functionally distinct proteins. For example, in this instance, the term "OX-2" and "CD200" is used in the relevant art to identify OX-2 proteins from different species. Notably, Raheb et al (Immun. Lett., 68:311-315, 1999, IDS filed May, 22, 2006) teach that the OX-2 proteins from human, rat and mouse are structurally and functionally distinct proteins, since, for example, there are species specific antibodies to each OX-2 protein (see entire document, e.g., page 314, left column). Additionally, as some claims recite both "OX-2/CD200" and "CD200" it is unclear if these terms are meant to identify one and the same protein or two different proteins. Accordingly, because it is unclear and cannot be ascertained to which of the different proteins termed "OX-2/CD200" or "CD200" these claims are directed, it is submitted that the metes and bounds of the

subject matter that is regarded as the invention is not delineated with the clarity and particularity to satisfy the requirement set forth under 35 U.S.C. § 112, second paragraph, so as permit the skilled artisan to know or determine infringing subject matter.

It is suggested that this issue be remedied by amending the claims to recite a limitation requiring the "OX-2/CD200" or "CD200" protein to comprise a particular amino acid sequence (or other limitations that unambiguously identify the protein to which the claims are directed), which is disclosed in the specification, as filed, because such a limitation would serve to unambiguously identify the protein to which the claim is directed.

(b) Claims 1-3, 7-9, 13-15, 19-21 and 25-55 are indefinite because of the recitation in claims 1, 7, 13, 19, and 49-51 of the limitation, "the immune-suppressing effect of OX-2/CD200". This limitation renders the claims indefinite because it fails to point out with the requisite clarity and particularity what "effect" is considered the immune suppressing effect of OX-2/CD200. Notably, Gorczynski et al (J. Immun., 163:1654-1660, 1999, IDS filed May 22, 2006) teach that OX-2/CD200 proteins have multiple effects that suppress the immune system, including downregulating the pro-inflammatory cytokines IL-2 and IFN-γ and upregulating the anti-inflammatory cytokine IL-10. (see entire document, e.g., page 1658, Table 3). Accordingly, because it is unclear or cannot be ascertained to which effect these claims are directed, or which "effect" is considered "the immune-suppressing effect of OX-2/CD200", it is submitted that the metes and bounds of the subject matter that is regarded as the invention is not delineated with the clarity and particularity to satisfy the requirement set forth under 35 U.S.C. § 112, second paragraph, so as permit the skilled artisan to know or determine infringing subject matter.

14. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. Claims 1-3, 7-9, 13-15, 19-21 and 25-55 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a "written description" rejection.

The considerations that are made in determining whether a claimed invention is supported by an adequate written description are outlined by the published Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, para. 1, ``Written Description" Requirement (Federal Register; Vol. 66, No. 4, January 5, 2001; hereinafter "Guidelines"). A copy of this publication can be viewed or acquired on the Internet at the following address: <http://www.gpoaccess.gov/>.

These guidelines state that rejection of a claim for lack of written description, where the claim recites the language of an original claim should be rare. Nevertheless, these guidelines further state, "the issue of a lack of written description may arise even for an original claim when an aspect of the claimed invention has not been described with sufficient particularity such that one skilled in the art would recognize that the applicant has possession of the claimed invention" (*Id.* at 1105). The "Guidelines" continue:

> The claimed invention as a whole may not be adequately described if the claims require an essential or critical feature which is not adequately described in the specification and which is not conventional in the art or known to one of ordinary skill in the art. This problem may arise where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process.

With further regard to the proposition that, as *original* claims, the claims themselves provide *in haec verba* support sufficient to satisfy the written description requirement, the Federal Circuit has explained that *in ipsis verbis* support for the claims

in the specification does not *per se* establish compliance with the written description requirement:

> Even if a claim is supported by the specification, the language of the specification, to the extent possible, must describe the claimed invention so that one skilled in the art can recognize what is claimed. The appearance of mere indistinct words in a specification or a claim, even an original claim, does not necessarily satisfy that requirement. The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described. *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

Regents of the University of California v. Eli Lilly & Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). *See also:* University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 1892 (CA FC 2004).

Thus, an original claim may provide written description for itself, but it must still be an adequate written description, *which establishes that the inventor was in possession of the invention.*

(a) In the instant case, claims 1-3, 7-9, 13-15, 19-21 and 25-55 are drawn to methods comprising determining whether a member of a structurally and functionally diverse genus of "OX/CD200 proteins" is upregulated in a subject and then administering to subjects a member of a structurally and functionally diverse genus of "polypeptides or antibodies" that bind to the member of the structurally and functionally diverse genus of "OX/CD200 proteins" that is upregulated, wherein the polypeptide or antibody is administered in an amount effective to "inhibit the immune-suppressing effect of OX-2/CD200". Notably, while members of the genus of polypeptides that are administered to the subject are not necessarily antibodies, neither the proteins nor the antibodies that bind to OX2/CD200 necessarily comprise each of the 6 CDRs in the proper context of the light and heavy chain framework regions of an antibody that is known or recognized to bind human OX-2/CD200. Additionally, since the art teaches a polypeptide designated "OX-2/CD200" protein, which has multiple immune suppressing effects, it is submitted that the specification does not adequately describe the particular "immune suppressing effect of OX-2/CD200" that the "polypeptide or antibody" administered to the subject necessarily has.

As will be explained in further detail in the following paragraphs, the specification only adequately describes antibodies that specifically bind to the human OX-2/CD200 protein that comprise CDRs consisting of all of the 6 complementarity determining regions (CDRs) of the scFv-9 antibody, i.e., a light chain CDR1 region consisting of SEQ ID NO:12, a light chain CDR2 region consisting of SEQ ID NO:23, a light chain CDR3 region consisting of SEQ ID NO:37, a heavy chain CDR1 region consisting of SEQ ID NO:55, a heavy chain CDR2 region consisting of SEQ ID NO:74 and a heavy chain CDR3 region consisting of SEQ ID NO:93 as antibodies that inhibit the downregulation of IL-2 and IFN-γ by human OX-2/CD200.

To elaborate on this point, Mariuzza et al. (*Annu. Rev. Biophys. Biophys. Chem.* 1987; **16**: 139-159) reviews the structural basis of antigen-antibody recognition and teaches that a naturally occurring antibody comprises two polypeptides, the so-called light and heavy chains. The antigen-combining site of an antibody is a three-dimensional structure, which fully comprises six "complementarity-determining regions" (CDRs), three each from the light and heavy chains. The amino acid sequences of the CDRs are hypervariable, as the amino acid residues contained within the CDRs determine much of antibody's antigen-binding specificity. Of the amino acid residues of the antibody contacting the antigen, six are within the light chain, nine are within the heavy chain, and two are within the constant or nearly constant "framework" regions.

In view of Mariuzza et al., it is apparent that having only described one of the six CDRs that form the antigen binding site of an antibody does not suffice to describe the particularly identifying structural feature of the antibody that correlates with the antibody's ability to bind to the antigen. Absent a description of the at least minimal structural features correlating with a functional ability to bind to a particular antigen, which are shared by members of a genus commonly sharing this function, it is submitted that the skilled artisan could not immediately envision, recognize or distinguish members of the genus from other antibodies or other proteins that bind OX2/CD200, which are not antibodies. Proteins (e.g., peptides), which are not antibodies but function as ligands of OX2/CD200, need not have any particular structure; therefore, there is no correlation between their common ability to bind

OX2/CD20 and any one particularly identifying structural feature that commonly characterizes such proteins, and again the skilled artisan could not immediately envision, recognize or distinguish these proteins to which the claims are directed. For this reason, the specification would not reasonably convey to the skilled artisan that Applicant had possession of the claimed invention at the time the application was filed.

Furthermore, the specification only describes antibodies comprising 3 CDRs of a heavy chain in a heavy chain framework and three CDRs of a light chain in a light chain framework as antibodies or polypeptides that specifically bind to human Ox-2/CD200. For example, figure 9b of the specification discloses that the scFv antibody clone E2c (also referred to in the specification as scFv-9), comprises a light chain CDR1 region consisting of SEQ ID NO:12, a light chain CDR2 region consisting of SEQ ID NO:23, a light chain CDR3 region consisting of SEQ ID NO:37, a heavy chain CDR1 region consisting of SEQ ID NO:55, a heavy chain CDR2 region consisting of SEQ ID NO:74 and a heavy chain CDR3 region consisting of SEQ ID NO:93 and figure 13 and page 25 disclose that this antibody specifically binds a human antigen expressed on human CLL-AAT cells that was identified as human OX-2/CD200. Notably, while the specification discloses two other antibodies, i.e., scFv-4 and scFv-10 that selectively bind cells transfected with human OX-2/CD200 (see figure 13), the specification only provides evidence that an antibody containing all 6 CDRs of the scFv-9 antibody inhibits the downregulation of IL-2 and IFN-γ caused by expression of OX-2/CD200 in transfected cells by blocking human OX-2/CD200 from binding its receptor (see Figures 14-16 and page 29).

Notably, one of skill in the art would not conclude that the scFv-9 antibody that binds human OX-2/CD200 protein is representative of all antibodies that bind any OX-2/CD200 protein as Raheb et al (Immun. Lett., 68:311-315, 1999, IDS filed May 22, 2006) teach that there are species specific OX-2/CD200 antibodies for the OX-2/CD200 proteins from human, rat and mouse (see entire document, e.g., page 314, left column). Furthermore, Chen et al (Transplantation, 79:282-288, 2005, IDS filed October 2, 2006) teach that only antibodies that specifically bind to human OX-2/CD200 in its N-terminal region have the ability to inhibit the down regulation of IL-2 by human OX-2/CD200 (see

entire document, e.g., page 286, Figure 5B), while antibodies that specifically bind in the C-terminal region do not have this ability. Finally, Gorczynski et al (J. Immun., 163:1654-1660, 1999, IDS filed May 22, 2006) teach that OX-2/CD200 proteins cause multiple effects that suppress the immune system, including downregulating IL-2 and IFN-γ. Furthermore, Gorczynski et al teach that OX-2 proteins also upregulate the anti-inflammatory cytokine IL-10 (see entire document, e.g., page 1658, Table 3).

Therefore, the specification does not teach any polypeptides that are not antibodies capable of binding to OX-2/CD200 that comprise CDRs of the described antibodies, and one of skill in the art would not immediately envision or recognize that polypeptides consisting of, for example, just one CDR of these scFv antibodies or even polypeptides consisting of all 6 CDRs that were not in the proper context of their antibody frameworks would retain the ability to bind to OX-2/CD200.

Thus, one of skill in the art would only immediately envision or recognize that the scFv-9 antibody would necessarily specifically bind the human OX-2/CD200 protein and would only immediately envision or recognize that the scFv-9 antibody has the ability to downregulate IL-2 and IFN-γ caused by human OX-2/CD200. Therefore, one of skill in the art would not conclude that applicant was in possession of the genus of "polypeptides or antibodies that bind any OX-2/CD200 protein that can inhibit any immune-suppressing effect of OX-2/CD200".

In this case, the specification only adequately describes antibodies comprising all 6 CDRs of the scFv-9 clone as antibodies that specifically bind human OX-2/CD200 and have the effect of downregulating IL-2 and IFN-γ caused by upregulated expression of human OX-2/CD200. While the prior art teaches well-known and conventional methodology for CDR grafting heavy and light chain CDRs into corresponding heavy and light chain frameworks to create "humanized" or "chimeric" antibodies that would be expected to retain the ability of the antibody comprising all 6 CDRs of the scFv-9 clone to block binding of human OX-2/CD200 to its receptor, one of skill in the art would not immediately envision or recognize which polypeptide or antibodies comprising less than all 6 CDRs of a parent antibody in the proper context of heavy and light chain

frameworks would retain the binding affinity and specificity of the parent antibody and would not conclude that, for example, an antibody that binds OX-2/CD200, from another species or even an antibody that binds human OX-2/CD200 would have the ability to "inhibit the immune suppressing effect of OX-2/CD200".

For example, Gussow et al. (Meth. in Enzy. 1991; 203: 99-121) teach the general methodology for making humanized antibodies; see entire document. One means for producing a humanized antibody involves grafting the six CDRs from the light and heavy chain variable regions from a murine antibody into the framework of a human antibody. However, in general, if only one or two of the CDRs from either the light or heavy chain variable region were to be grafted, but not all three, the resultant antibody would not be expected to retain the binding affinity and specificity of the parent antibody. Therefore, since it is expected that all 6 CDRs need to be grafted into antibody framework regions to retain the requisite affinity and specificity of the parent antibody, polypeptides or antibodies that do not comprise all 6 CDRs grafted into framework regions, i.e., are not antibodies that contain all 6 CDRs of the parent antibody, would not be immediately envisioned or recognized by one of skill in the art as having the affinity and specificity of the parent antibody required to retain the ability to down regulate IL-2 and IFN-γ..

The Federal Circuit has decided that a patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated. See *Noelle v. Lederman*, 69 USPQ2d 1508 1514 (CA FC 2004) (citing *Enzo Biochem II*, 323 F.3d at 965; *Regents*, 119 F.3d at 1568).

Additionally, "generalized language may not suffice if it does not convey the detailed identity of an invention." *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1892 (CAFC 2004).

Although the skilled artisan could potentially screen candidate polypeptides or antibodies comprising only the heavy chain variable region CDR3 of SEQ ID NO: 93, for example, or alternatively candidate anti-OX-2/CD200 antibodies to identify those that

are capable of "inhibiting the downregulation of IL-2 and IFN-γ caused by OX-2/CD200, it is duly noted that the written description provision of 35 U.S.C § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it.

> The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the "written description" inquiry, *whatever is now claimed.*

Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (CAFC 1991). See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993); *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.,* 18 USPQ2d 1016 (CAFC 1991); *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1892 (CAFC 2004).

"Guidelines" states, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (*Id.* at 1104). Moreover, because the claims are directed to a genus of structurally disparate polypeptides and antibodies that are capable of inhibiting the immune-suppressing effect of OX-2/CD200, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. In this instance, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; Applicant has not shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; and Applicant has not described distinguishing identifying characteristics sufficient to show that Applicant was in possession of the claimed invention at the time the application was filed.

It is not sufficient to define a substance solely by its principal biological property, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property. Per the *Enzo* court's example, (*Enzo Biochem, Inc. v. Gen-Probe Inc.*, 63 USPQ2d 1609 (CA FC 2002) at 1616) of a description of an anti-inflammatory steroid, i.e., a steroid (a generic structural term) couched "in terms of its function of lessening inflammation of tissues" which, the court stated, "fails to distinguish any steroid from others having the same activity or function". Similarly, the function of "inhibiting the immune-suppressing effect of OX-2/CD200" does not distinguish polypeptides of antibodies, from others having the same activity or function and as such, fails to satisfy the written-description requirement. Applicant has not disclosed any relevant, identifying characteristics, such as structure or other physical and/or chemical properties, sufficient to show possession of the claimed genus. Mere idea or function is insufficient for written description; isolation and characterization at a minimum are required. A description of what a material does, rather than what it is, usually does not suffice. *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

Given the lack of particularity with which the OX-2/CD200 protein and polypeptides or antibodies that bind OX-2/CD200, to which the claims are directed, are described in the specification, it is submitted that the skilled artisan could not immediately envision, recognize or distinguish at least most of the members of the genus of "polypeptides or antibodies that bind OX-2/CD200" that have the ability to "inhibit the immune suppressing effect of OX-2/CD200", to which the claims are directed; and therefore the specification would not reasonably convey to the skilled artisan that Applicant had possession of the claimed invention at the time the application was filed.

(b) In this instance, the claims 1-3, 7-9, 13-15, and 25-42, 49-50 and 52-55 are directed to a methods of treatment drawn to "any subject in which CD200 is upregulated" (see e.g., claim 1), "any subject afflicted with a disease state in which OX-

2/CD200 is upregulated" (see e.g., claim 7) or "any subject afflicted with cancer in which CD200 is upregulated" (see e.g., claim 13).

However, in this case the specification only adequately describes patients afflicted with chronic lymphocytic leukemia as subjects in which CD200 is upregulated.

Notably, the specification only discloses that the human OX-2/CD200 protein is upregulated on a subset of subjects with chronic lymphocytic leukemia (CLL) tumors (see page 25 and Figure 8) and that CLL cells that overexpress OX-2/CD200 when treated with an scFv-9 antibody converted to full IgG downregulate IL-2 and IFN-γ production (see page 28). Notably, the specification does not disclose any other diseases, cancers or subjects in which CD200 is upregulated that could be treated with the claimed methods.

Furthermore, it is not apparent why certain chronic lymphocytic leukemia subjects that upregulate OX-2/CD200 should be considered representative of these genera, as a whole, because it is established in the art that not all subjects in which OX-2/CD200 is upregulated will benefit from treatments that inhibit OX-2/CD200.

Supporting the assertion that chronic lymphocytic leukemia subjects in which CD200 is upregulated are not representative of the genera of "subjects", "disease subjects" or "cancer subjects" in which CD200 is upregulated, as a whole, Wilczynski et al (Human Immun., 67:492-511, 2006) teach that CD200 is upregulated in mice that display increased graft tolerance likely in order to prevent graft rejection (see entire document, e.g., page 494, left column). Additionally, Chitnis et al (Am. J. Pathol. 170(5):1695-1712, 2007) teach that elevated neuronal expression of CD200 attenuates the disease course of experimental autoimmune encephalomyelitis (EAE) (See entire document, e.g., abstract). Accordingly, treating these "subjects with upregulated OX-2/CD200" disclosed by Wilczynski et al and Chitnis et al with an antibody that inhibits the OX-2/CD200 protien would be expected to be detrimental to these "subjects".

Furthermore, Kretz-Rommel et al (J. Immunology, 178:5595-5605, 2007) teach that CD200 is not upregulated on the Raji and Namalwa Burkitt's lymphoma cancer cell lines (see entire document, e.g., page 5598, left column).

Therefore, if the upregulation of OX-2/CD200 is beneficial to some subjects and detrimental to other subjects and OX-2/CD200 is upregulated in some cancers, but not others, it stands to reason that one cannot predict which of the "subjects with upregulated OX-2/CD200" encompassed by the claims would benefit from treatments that inhibit OX-2/CD200. For these reasons, the skilled artisan could not immediately envision, recognize or distinguish the "subjects", "disease subjects" or "cancer subjects" in which CD200 is upregulated to which the claims are directed; and as such the specification would not reasonably convey to the skilled artisan that Applicant had possession of the claimed invention at the time the application was filed.

For these reasons, the skilled artisan could not immediately envision, recognize or distinguish which "subjects in which CD200 is upregulated", which "subjects afflicted with a disease state in which OX-2/CD200 is upregulated" or which "subjects afflicted with cancer in which CD200 is upregulated" could be treated with the claimed methods; and as such the specification would not reasonably convey to the skilled artisan that Applicant had possession of the claimed invention at the time the application was filed.

"[G]eneralized language may not suffice if it does not convey the detailed identity of an invention." *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1892 (CAFC 2004). In this instance, there is no language that adequately describes which subjects could be treated with the claimed methods.

16. Claims 1-3, 7-9, 13-15, 19-21 and 25-55 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

MPEP § 2164.01 states:

> The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Accordingly, even though the statute does not use the term "undue experimentation," it has been interpreted to require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors, which have been outlined in the Federal Circuit decision of *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), include, but are not limited to, the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed. See also *Ex parte Forman*, 230 USPQ 546 (BPAI 1986).

The amount of guidance, direction, and exemplification disclosed in the specification, as filed, would not be sufficient to enable the skilled artisan to make and/or use the claimed invention at the time the application was filed without undue and/or unreasonable experimentation.

The claims are herein drawn to methods of treating subjects with upregulated CD200 with an antibody comprising the 6 CDRs of the scFv-9 antibody, i.e., a light chain CDR1 region consisting of SEQ ID NO:12, a light chain CDR2 region consisting of SEQ ID NO:23, a light chain CDR3 region consisting of SEQ ID NO:37, a heavy chain CDR1 region consisting of SEQ ID NO:55, a heavy chain CDR2 region consisting of SEQ ID NO:74 and a heavy chain CDR3 region consisting of SEQ ID NO:93.

Notably, the specification only discloses that the scFv-9 antibody binds to human OX-2/CD200, that human OX-2/CD200 is upregulated in some patients with B-cell chronic lymphocytic leukemia and that an antibody comprising the 6 CDRs of the scFv-9 antibody *in vitro* can inhibit IL-2 and IFN-γ production of CLL cells. Notably, the

specification provides no evidence or scientific reasoning that would suggest that antibodies comprising the 6 CDRs of the scFv-9 antibody inhibit tumor growth *in vitro* or *in vivo* and does not provide any other evidence that inhibiting IL-2 and IFN-γ production of CLL cells would be useful to treat any disease.

Therefore, the specification does not enable methods of treating subjects with upregulated OX-2/CD200 with an antibody comprising the 6 CDRs of the scFv-9 antibody.

Notably, as explained in the above rejection of the claims as lacking adequate written description subjects that have undergone graft transplants and subjects with other diseases are known to upregulate OX-2/CD200 and therefore one of skill in the art would be subject to undue experimentation to practice the claimed methods as it appears that not all subjects with upregulated OX-2/CD200 could be treated with the claimed methods.

Furthermore, where the claims are drawn to methods with no intended use, see e.g., claim 1, one of skill in the art would be subject to undue experimentation to determine a use for the claimed methods.

Finally, since the specification does not provide any specific non-general guidance as to how to treat CLL patients with upregulated OX-2/CD200 with an antibody comprising the 6 CDRs of the scFv-9 antibody, the specification does not enable methods of treating CLL comprising administering to CLL subjects with upregulated OX-2/CD200 an antibody comprising the 6 CDRs of the scFv-9 antibody as one of skill in the art would be subject to undue experimentation to practice such methods.

The state of the art was such that those of skill in the art readily recognized the unpredictability of extrapolating *in vitro* cell line data or mouse xenograft model data to human treatments, even when the extrapolation was from the same product tested *in vitro* or in the mouse tumor model to its use as a human tumor treatment. With particular regard to anticancer drug discovery, Gura (*Science*. 1997; **278**: 1041-1042), for example, teaches that researchers are faced with the problem of sifting through potential anticancer agents to find ones promising enough to make human clinical trials

worthwhile (abstract). Because of a lack of predictability, Gura discloses that often researchers merely succeed in developing a therapeutic agent that is useful for treating the cell that has been used as a model, but which is ineffective in humans, and indicates that the results acquired during pre-clinical studies are often non-correlative with the results acquired during clinical trials (page 1041, column 2). Additionally, Zips et al (in vivo, 19:1-7, 2005) teach that "[u]nlike the situation *in vitro*, a tumor is a 3-dimensional complex consisting of interacting malignant and non-malignant cells", so predicting the effect of an anticancer agent *in vivo* based on *in vitro* data is not reliable (see page 3, right column). Additionally, Dennis (Nature, 442:739-741, August 2006) states "human cells are likely to behave differently in a mouse than in a human body, making results hard to interpret) (see page 739, middle column) and that "interactions between tumour cells and their neighbors are often lost in xenografts, because proteins from one species can't interact with their counterparts in the host" (see page 740, third column). Furthermore, Srivastava (Nature Immunology, 1(5):363-366, November 2000) teaches that "the human cancers that we aim to treat are well established and have taken their time getting there", while the mouse models used are often "established for anything from a few hours to less than a week before treatment" and that mouse models "must show some semblance to the human disease to be credible" (see page 365, right column). Thus, since the specification does not provide any specific non-general guidance as to use an antibody comprising the 6 CDRs of the scFv-9 antibody to treat patients with upregulated OX-2/C200, one of skill in the art would be subject to undue experimentation to determine if is such antibodies could treat patients afflicted with CLL with upregulated OX-2/CD200.

Notably, since it is highly unpredictable in the art to even extrapolate mouse xenograft cancer model data to human treatments, one of skill in the art would be subject to undue experimentation to use antibodies comprising the 6 CDRs of the scFv-9 antibody to treat patients with upregulated OX-2/CD200 as the instant specification only provides *in vitro* evidence that an antibody comprising the 6 CDRs of the scFv-9 antibody can inhibit IL-2 and IFN-γ production in CLL cells that overexpress OX-2/CD200. Furthermore, since the specification has not established a correlation

between this reduction of IL-2 and IFN-γ production in CLL cells that overexpress OX-2/CD200 with any effect on CLL tumor growth either *in vitro* or *in* vivo one of skill in the art would be subject to undue experimentation to use antibodies comprising the 6 CDRs of the scFv-9 antibody to treat patients with upregulated OX-2/CD200.

In view of the evidence of the lack of the predictability of the art to which the invention pertains, the lack of guidance and direction providing a specific and detailed description in applicant's specification of how to effectively use an antibody comprising the 6 CDRs of the scFv-9 antibody to treat subjects in which OX-2/CD200 is upregulated, undue experimentation would be required to practice the full scope of the claimed invention.

Applicant is reminded that reasonable correlation must exist between the scope of the claims and scope of enablement set forth.

In deciding *In re Fisher*, 166 USPQ 18, 24 (CCPA 1970), the Court indicated the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. "Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention." *Genentech Inc. v. Novo Nordisk A/S*, 42 USPQ2d 1001, 1005 (CA FC 1997).

In summary, the specification would not have enabled the skilled artisan to use the disclosed and claimed methods comprising administering to those subjects in which CD200 is upregulated an antibody comprising the 6 CDRs of the scFv-9 antibody without undue and/or unreasonable experimentation. The specification would not have enabled the use of methods of treating a disease state comprising administering to those subjects afflicted with a disease state in which CD200 is upregulated an antibody comprising the 6 CDRs of the scFv-9 antibody. The specification would not have enabled the use of methods of treating cancer comprising administering to those cancer subjects in which CD200 is upregulated an antibody comprising the 6 CDRs of the scFv-9 antibody. Finally, the specification would have not enabled the use of methods

of treating chronic lymphocytic leukemia (CLL) comprising administering to those CLL subjects in which CD200 is upregulated an antibody comprising the 6 CDRs of the scFv-9 antibody.

Therefore, in conclusion, upon careful consideration of the factors used to determine whether undue experimentation is required, in accordance with the Federal Circuit decision of *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the amount of guidance, direction, and exemplification disclosed in the specification, as filed, is not deemed sufficient to have enable the skilled artisan to make and/or use the claimed invention at the time the application was filed without undue and/or unreasonable experimentation.

Double Patenting

17. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

18. Claims 1-3, 7-9, 13-15, 19-21 and 49-55 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims

50-54 of copending Application No. 10/379,151. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 50-54 of copending Application No. 10/379,151 are so substantially similar that for the most part, the claimed subject matter of the copending application anticipates the claimed subject matter of the instant application and any minor differences in the subject matter claimed in the instant application would be seen as an obvious variation of the subject matter claimed in the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The instant claims are described supra.

Claims 50-54 of copending Application No. 10/379,151 are drawn to methods of treating chronic lymphocytic leukemia comprising administering to a patient suffering from CLL with upregulated OX-2/CD200 an antibody that specifically binds to OX-2/CD200. While the methods of the copending claims do not expressly comprise a step by which the practitioner determines if OX-2/CD200 is upregulated in a subject, it would be immediately obvious to one of ordinary skill in the art that the method would necessarily involve the prior determination that OX-2/CD200 is upregulated in the subject, since the method comprises administering the antibody to patients wherein OX-2/CD200 is upregulated by CLL cells.

Accordingly, the claimed inventions are so substantially similar that for the most part, the claimed subject matter of the copending application anticipates the claimed subject matter of the instant application and any minor differences in the subject matter claimed in the instant application would be seen as an obvious variation of the subject matter claimed in the copending application.

19. Claims 1-3, 7-9, 13-15, 19-21 and 49-55 are directed to an invention not patentably distinct from claims 50-54 of commonly assigned application 10/379,151. Specifically, although the conflicting claims are not identical, they are not patentably distinct from each other for the reasons set forth in the above provisional rejection of the claims on the ground of nonstatutory obviousness-type double patenting.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned copending application 10/379,151, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

Conclusion

20. No claims are allowed.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brad Duffy whose telephone number is (571) 272-9935. The examiner can normally be reached on Monday through Friday 7:00 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Respectfully,
Brad Duffy
571-272-9935

/Stephen L. Rawlings/
Stephen L. Rawlings, Ph.D.
Primary Examiner, Art Unit 1643

bd
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